

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
9 June 2005 (09.06.2005)

PCT

(10) International Publication Number
WO 2005/052006 A3

(51) International Patent Classification⁷: C07K 16/28,
19/00, C12N 15/13, 15/62, A61K 39/395, C07K 14/21,
A61K 47/48

(21) International Application Number:
PCT/US2004/039617

(22) International Filing Date:
24 November 2004 (24.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/525,371 25 November 2003 (25.11.2003) US

(71) Applicant (for all designated States except US): THE
GOVERNMENT OF THE UNITED STATES, AS RE-
PRESENTED BY THE SECRETARY OF HEALTH
AND HUMAN SERVICES [US/US]; Office of Tech-
nology Transfer, 6011 Executive Boulevard, Suite 325,
Rockville, MD 20852-3804 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): PASTAN, Ira H.

[US/US]; 11710 Beall Mountain Road, Potomac, MD
20854 (US). HIO, Mitchell [US/US]; 13859 Grey Colt
Drive, North Potomac, MD 20878 (US). BANG, Sook-Hee
[KR/US]; 6030 California Circle, #104, Rockville, MD
20852 (US).

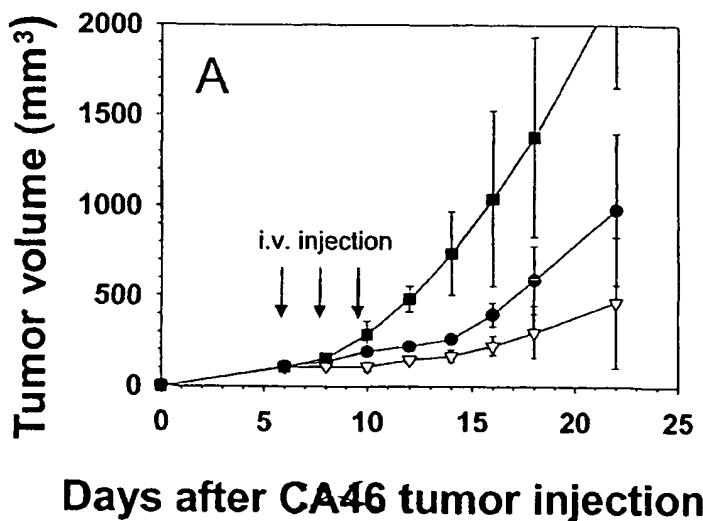
(74) Agents: LOCKYER, Jean M. et al.; Townsend and
Townsend and Crew LLP, 2 Embarcadero Center, 8th
Floor, San Francisco, CA 94111 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,

[Continued on next page]

(54) Title: MUTATED ANTI-CD22 ANTIBODIES AND IMMUNOCONJUGATES



(57) Abstract: Recombinant immunotoxins are fusion proteins composed of the Fv domains of antibodies fused to bacterial or plant toxins. RFB4 (Fv)-PE38 is an immunotoxin that targets CD22 expressed on B cells and B cell malignancies. The present invention provides antibodies and antibody fragments that have improved ability to bind the CD22 antigen compared to RFB4. Immunotoxins made with the antibodies and antibody fragments of the invention have improved cytotoxicity to CD22-expressing cancer cells. Compositions that incorporate these antibodies into chimeric immunotoxin molecules that can be used in medicaments and methods for inhibiting the growth and proliferation of such cancers. Additionally, the invention provides a method of increasing the cytotoxicity of forms of Pseudomonas exotoxin A ("PE") with the mutation of a single amino acid, as well as compositions of such mutated PEs, nucleic acids encoding them, and methods for using the mutated PEs.

WO 2005/052006 A3

